Shared care protocol

Hydroxychloroquine for patients within adult services

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Version	Date published	Changes since previous version
RDTC v1.0	14th February 2024	• Hyperlinks and references updated to current versions. • Advice added as per MHRA Drug Safety Update on psychiatric and cardiovascular adverse events • Links added to RMOC document on hydroxychloroquine and chloroquine retinopathy monitoring • Advice on shingles vaccination updated to reflect new national schedule
RDTC v1.1	26th November 2024	• Advice on shingles vaccine clarified to reflect potential eligibility of patients aged 50 years or older taking immunosuppressive therapy

Local review and adoption

Local approval	Date
Local content added	August 2024
Approved for use by Humber and North Yorkshire ICB	

Clinical content has been reviewed and updated by the RDTC on the date indicated above. Every effort is made to keep the content up to date. These templates are provided to the North West and North East and Yorkshire ICBs for localisation and approval through standard ICB processes. The most recent version is available on the RDTC website at https://rdtc.nhs.uk/prescribing-support-document/shared-care-protocol-hydroxychloroquine-for-adults.

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Shared Care Protocol

Hydroxychloroquine for patients within adult services

1. Background	Hydroxychloroquine is an antimalarial and a disease modifying anti-rheumatic drug (DMARD) with several pharmacological actions which may be involved in its therapeutic effect. Hydroxychloroquine is not licensed for all indications included in this shared care protocol. Its use for the indications below is however supported by various sources and bodies including the BNF, NICE, British Society for Rheumatology (BSR) and British Health Professionals in Rheumatology (BHPR), British Association of Dermatologists (BAD) and British Thoracic Society (BTS).
2. Licensed and agreed off-label indications	Hydroxychloroquine is licensed for treatment of: • Active rheumatoid arthritis • Systemic and discoid lupus erythematosus • Dermatological conditions caused or aggravated by sunlight This shared care protocol also includes treatment of chronic inflammatory conditions where off-label use of hydroxychloroquine is appropriate, including but not limited to the following specialities and conditions: • Rheumatology (e.g. inflammatory arthritis, connective tissue disease, Sjögren's syndrome, myositis) • Dermatology (e.g. urticaria, other inflammatory skin diseases) • Respiratory disease (e.g. interstitial lung disease, sarcoidosis). • Renal medicine These additional indications are off-label. **The initiating specialist must specify the indication for each patient when initiating shared care and clearly state when use is off-label.** This shared care protocol applies to adults aged 18 and over.
3. Locally agreed indications	Rheumatoid arthritis and inflammatory osteoarthritis Discoid and systemic lupus erythematosus Dermatological conditions caused or aggravated by sunlight
4. Initiation and ongoing dose regime	Transfer of monitoring and prescribing to primary care is normally after at least 4 weeks following initiation on the basis that the patient's dose has been optimised and has satisfactory investigation results. The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability. All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician. Termination of treatment will be the responsibility of the specialist. **Initial dosing:** 200mg to 400 mg daily. Dose should not exceed 6.5 mg/kg/day (based on actual body weight).

	Prescribing during the initial period must be by the initiating specialist – usually this is 4 weeks. Actual body weight is recommended to be used here to avoid excessive dosage in underweight patients. To avoid excessive dosage in obese patients, the dose of hydroxychloroquine should be calculated on the basis of ideal body-weight. **Maintenance dose (following initial stabilisation):** 200mg to 400 mg daily. The risk of significant toxicity increases with doses above 5 mg/kg/day (based on actual body weight). **The initial maintenance dose must be prescribed by the initiating specialist.** **Conditions requiring dose adjustment:** In patients taking 400mg daily, the dose can be reduced to 200mg when no further improvement is evident. The maintenance dose may be increased to 400mg daily if the response lessens. Dose adjustment and caution are recommended in renal or hepatic impairment.
5. Baseline investigations, initial monitoring, and ongoing monitoring to be undertaken by specialist	Monitoring at baseline and during initiation is the responsibility of the specialist; only once the patient is optimised on the chosen medication and dose with no anticipated further changes expected in the immediate future will prescribing and monitoring be transferred to primary care. **Baseline investigations:** • Urea and electrolytes (U&Es) & creatinine clearance (CrCl) • Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST), & albumin • Full blood count (FBC) • Weight • Height and blood pressure (if indicated) • Assess for co-morbidities which may influence DMARD choice, including risk factors for retinopathy (e.g. concomitant tamoxifen use, eGFR <60 mL/min) • Electrocardiogram (ECG), if concerns exist regarding the QT-interval, see section 8 and section 9. **Ongoing monitoring:** • No routine ongoing laboratory monitoring is required for hydroxychloroquine. Monitoring may be required if the patient is prescribed an additional DMARD. • The specialist will retain the responsibility for monitoring the patient's ongoing response to treatment, and advise if a dose change or treatment cessation is appropriate. This should be undertaken annually. • After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 6 remains appropriate. • After the patient has been on hydroxychloroquine for five years, refer to ophthalmology (see Appendix 1) for annual monitoring for retinopathy. Patients who are at higher risk of retinal toxicity will need to be referred earlier. See section 6 below for risk factors.

6. Ongoing monitoring requirements to be undertaken by primary care

If monitoring results are forwarded to the specialist team, please include clear clinical information on the reason for sending, to inform action to be taken by secondary care.

Monitoring	**Frequency**
Remind the specialist when the patient is approaching **5 years of treatment** (or **1 year** in patients with additional risk factors). These patients require referral from the specialist to ophthalmology (or other commissioned service as appropriate) for annual retinopathy monitoring. See RCOphth guidelines and RMOC Hydroxychloroquine and chloroquine retinopathy monitoring.. Risk factors may change over time; primary care should discuss with specialist if new risk factors that are 'high risk' are identified before the five-year mark.	• Annually after 5 years of treatment, **or** • After 1 year if additional risk factors are present. Risk factors include: ○ concomitant tamoxifen use ○ impaired renal function (eGFR <60mL/min/1.73m^2) ○ hydroxychloroquine dose (>5mg/kg/day) SystemOne searches are available to support practices in identifying patients requiring retinal monitoring and those at higher risk
• Patients aged 60-79 years old could be eligible for the shingles vaccine (herpes zoster). Patients aged 50 years or older and taking immunosuppressive therapy may also be eligible. Specialist input may be required. If patient is taking additional DMARDs, check advice for all drugs. For more information refer to Green Book Chapter 6 (Contraindications and special considerations) and ~~see~~ The Green Book, Chapter 28a. • Annual influenza (The Green Book, Chapter 19) vaccinations are recommended. • COVID-19 vaccination is safe and recommended (see The Green Book, Chapter 14a).	• Shingles vaccination: single course (two doses). • Influenza vaccination: annual. It is advisable to add the patient to the influenza vaccine list. • COVID-19 vaccination as per national schedule.

7. Pharmaceutical aspects

Route of administration:	Oral
Formulation:	Hydroxychloroquine sulfate 200 mg tablets. 300mg tablets are available but do not offer a clinical advantage and are not preferred. As an alternative, alternate day dosing with 200 mg and 400 mg may be used.

Administration details:	Each dose should be taken with food. If necessary, tablets may be crushed and dispersed in water (unlicensed).
Other important information:	Antacids may reduce absorption of hydroxychloroquine. Oral antacids should be avoided for 4 hours before and after the dose.

8. Cautions and contraindications	This information does not replace the Summary of Product Characteristics (SPC), and should be read in conjunction with it. Please see BNF & SPC for comprehensive information. **Contraindications:** • Hypersensitivity to hydroxychloroquine or 4-aminoquinoline compounds • Pre-existing maculopathy **Cautions:** • Concurrent use of medicines which may cause adverse ocular or skin reactions • Diabetes mellitus, and those taking anti-diabetic drugs (including SGLT-2 inhibitors) for any indication (hydroxychloroquine treatment may lower blood glucose) • Glucose-6-phosphate dehydrogenase deficiency • Increased risk of retinopathy with high doses (>5 mg/kg/day), long-term treatment (>5 years), eGFR <60 mL/min/1.73m^2 or concurrent tamoxifen use. • Myasthenia gravis or psoriasis (may exacerbate) • Porphyria cutanea tarda, and other acute porphyrias • Renal or hepatic disease and concurrent use of drugs known to affect these organs • Sensitivity to quinine • Severe gastrointestinal, neurological (especially for those with a history of epilepsy – may lower the seizure threshold), or blood disorders • Significant cardiac arrhythmias due to the risk of QT interval prolongation • Suicidal behaviour and psychiatric disorders have been reported in some patients treated with hydroxychloroquine, typically in the first month of treatment and including patients with no prior psychiatric history.
9. Significant drug interactions	The following list is not exhaustive. Please see BNF and SPC for comprehensive information and recommended management. **The following drugs must not be prescribed without consultation with the specialist:** • Drugs that can prolong the QT interval: for example, amiodarone, dronedarone, ranolazine, aripiprazole, chlorpromazine, haloperidol, erythromycin, moxifloxacin, quinine, citalopram, escitalopram, ondansetron,

	tolterodine. Avoid concomitant use; possible increased risk of QT prolongation/ventricular arrhythmias. • Cimetidine: possible increase in plasma concentration of hydroxychloroquine. • Ciclosporin: possible increase in plasma concentration of ciclosporin (combination used by some specialists). • Mefloquine and other drugs known to lower the convulsion threshold: possible increased risk of convulsions. • Penicillamine: possible increased risk of haematological toxicity. • Tamoxifen: increased risk of retinal toxicity, necessitates annual ophthalmic monitoring (see section 6). **The following drugs may be prescribed with caution:** • Macrolide antibiotics (e.g. azithromycin, erythromycin, clarithromycin): increased risk of cardiovascular events and cardiovascular mortality. Carefully consider the benefits and risks before prescribing this combination. See MHRA advice. • Antidiabetic drugs and/or insulin: hypoglycaemic effect may be enhanced, may need dose adjustment of antidiabetic medication. • Digoxin: possible increase in plasma concentration of digoxin. • Antacids and calcium carbonate-containing supplements: may reduce absorption of hydroxychloroquine; separate administration by at least four hours. Other calcium salts do not appear to interact. • Antiepileptics: activity of antiepileptic drugs may be impaired with hydroxychloroquine. Additionally, hydroxychloroquine may lower the seizure threshold. • Neostigmine and pyridostigmine: effects may be antagonised by hydroxychloroquine. • Intra-dermal rabies vaccine: possible reduced antibody response

10. Adverse effects and management

As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance**.** For information on incidence of ADRs see relevant SPCs.

Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit www.mhra.gov.uk/yellowcard.

Advice based on shared care guidelines published by NHS England, and checked against current guidance.

Adverse effect	Management
Retinopathy monitoring: possible or definite retinal toxicity	• **Possible retinopathy:** Consider whether withholding is in the best interests of the patient (See RCOphth guidelines for recommendations on managing possible retinopathy), specialist to be informed and to determine follow-up plan. • **Definite retinopathy:** primary care to ensure **withheld** pending urgent discussion between patient and specialist.
Vision disturbances including blurred vision, changes in visual acuity or abnormal colour vision	Refer to optometrist/ ophthalmologist; discuss with specialist team
Symptoms or signs of cardiomyopathy e.g. breathlessness, swelling in the abdomen and ankles, palpitations, cardiac conduction disorders and ECG changes.	Review for reversible causes. Discuss with specialist team urgently and consider withholding. If cardiomyopathy occurs due to hydroxychloroquine treatment, hydroxychloroquine must be withheld.
Headache, gastrointestinal disturbances e.g. abdominal pain, nausea, diarrhoea, vomiting	Review for reversible causes; discuss with specialist team if persistent or severe
Skin and subcutaneous tissue disorders e.g. pruritic erythematous macular rash occurring soon after treatment commenced, blue-black pigmentation of the skin, bleaching of skin & hair	Withhold and discuss with specialist team
Skeletal muscle myopathy or neuromyopathy	Review for reversible causes; withhold and discuss with specialist team
Signs and symptoms of bone marrow suppression e.g. sore throat, oral ulceration, abnormal bleeding/bruising, signs of infection	Review for reversible causes. Be aware that the underlying condition may contribute to bone marrow suppression. Although the risk is low, if bone marrow suppression is suspected, discontinue treatment and obtain an urgent FBC and other bloods as appropriate. Discuss with specialist team.
New or worsening mental health problems Including irrational thoughts, anxiety, hallucinations, and feeling confused or feeling depressed, including thoughts of self-harm or suicide	Manage as per local pathways. Discuss with specialist team.

11. Advice to patients and carers	**The patient should be advised to report any of the following signs or symptoms to their primary care prescriber without delay:** • Vision disturbances including blurred vision, changes in visual acuity or abnormal colour vision.

The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual drugs.	• Breathlessness, swelling in the abdomen or ankles, palpitations. • Headache, gastrointestinal disturbances e.g. abdominal pain, nausea, diarrhoea, vomiting. • Signs or symptoms of bone marrow suppression, such as a sore throat, oral ulceration, abnormal bleeding or bruising, or other signs of infection. • Rash, changes in skin or hair pigmentation. • Muscle weakness. • Symptoms of hypoglycaemia, including dizziness, weakness, or hunger. • Actual or planned pregnancy or breastfeeding. • Any new or worsening mental health problems, including irrational thoughts, anxiety, hallucinations, feeling confused or depressed, or thoughts of self harm or suicide. **The patient should be advised:** • Avoid over-the-counter and prescribed antacids for four hours before and after doses of hydroxychloroquine. • A number of patients who take hydroxychloroquine may experience some loss of their peripheral and central vision. Patients who drive must inform the DVLA if their eyesight is affected. For further information see: https://www.gov.uk/driving-eyesight-rules • That vaccination in line with current national advice (e.g. for COVID-19, influenza) is safe and recommended. • Tell anyone who prescribes them a medicine that they are taking hydroxychloroquine. Always ask a pharmacist before purchasing any medicines over the counter, including herbal or complementary remedies, and ask if they are safe. **Patient information:** • General information: patient.info • Rheumatology: Versus Arthritis • Dermatology: British Association of Dermatologists • Patient information leaflets are also available from electronic medicines compendium
12. Pregnancy, paternal exposure and breastfeeding	The BSR and BHPR guideline on prescribing DMARDs in pregnancy and breastfeeding advises the following: **Pregnancy:** Hydroxychloroquine can be continued throughout pregnancy. Information for patients and carers: Best Use of Medicines in Pregnancy. **Breastfeeding:** Hydroxychloroquine is compatible with breastfeeding, though does pass into breast milk in small quantities. Information for healthcare professionals: UK Drugs in Lactation Advisory Service .

	Paternal exposure: Hydroxychloroquine is compatible with paternal exposure.
13. Specialist contact information and arrangements for referral	**See clinic letter for contact details for responsible specialist** See Appendix 1 for retinal monitoring arrangements
14. Additional information	Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed. Ensure that the specialist is informed in writing of any changes to the patient's GP or their contact details.
15. References	1. British National Formulary. Accessed via https://bnf.nice.org.uk/ on 09/11/23 2. Hydroxychloroquine sulfate 200 mg film-coated tablets (Quinoric®). Bristol Laboratories. Date of revision of the text: 18/06/23. Accessed via https://www.medicines.org.uk/emc/product/477/smpc on 09/11/23 3. Hydroxychloroquine sulfate 200 mg film-coated tablets. Zentiva. Date of revision of the text: 27/06/23. Accessed via https://www.medicines.org.uk/emc/product/1764/smpc on 09/11/23 4. Hydroxychloroquine sulfate 200 mg film-coated tablets. Accord. Date of revision of the text: 24/06/2023. Accessed via https://products.mhra.gov.uk/ on 09/11/23. 5. Hydroxychloroquine sulfate 200 mg film-coated tablets. Blackrock Pharmaceuticals. Date of revision of the text: 15/11/2022. Accessed via https://www.medicines.org.uk/emc/product/11540/smpc on 09/11/23 6. Hydroxychloroquine sulfate 200 mg film-coated tablets. Ipca Laboratories. Date of revision of the text: 07/04/2020. Accessed via https://www.medicines.org.uk/emc/product/11516/smpc accessed on 09/11/23 7. British Society of Rheumatology and British Health Professionals in Rheumatology. 2017. Guidelines for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs. Accessed via https://academic.oup.com/rheumatology/article/56/6/865/3053478#97289292 . 8. British Society of Rheumatology and British Health Professionals in Rheumatology. 2022. British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding: immunomodulatory anti-rheumatic drugs and corticosteroids. Accessed via https://academic.oup.com/rheumatology/article/62/4/e48/6783012 9. British Thoracic Society in collaboration with the Thoracic Society of Australia and New Zealand and the Irish Thoracic Society. 2008. Interstitial lung disease guideline (archived). Accessed via https://www.brit-thoracic.org.uk/quality-improvement/guideline-archive/. 10. Renal Drug Database. Hydroxychloroquine sulphate. Reviewed 09/11/2023. Accessed via https://renaldrugdatabase.com/monographs/hydroxychloroquine-sulphate on 29/12/23. 11. Royal College of Ophthalmologists. 2020. Hydroxychloroquine and Chloroquine Retinopathy: Recommendations on Monitoring. Accessed via

	https://www.rcophth.ac.uk/standards-publications-research/clinical-guidelines/ on 09/11/23. 12. Immunisation against infectious diseases (The Green Book). Accessed via https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book on 09/11/23. 13. Stockley's Drug Interactions. Accessed via www.medicinescomplete.com on 09/11/23 14. NEWT Guidelines. Hydroxychloroquine. Last updated November 2012. Accessed via https://access.newtguidelines.com/H/Hydroxychloroquine.html on 09/11/23. 15. RMOC Hydroxychloroquine and chloroquine retinopathy monitoring. July 2022. https://www.england.nhs.uk/publication/hydroxychloroquine-and-chloroquine-retinopathy-monitoring/
16. To be read in conjunction with the following documents	• Shared Care for Medicines Guidance – A Standard Approach (RMOC). Available from https://www.sps.nhs.uk/articles/rmoc-shared-care-guidance/ • NHSE guidance – Responsibility for prescribing between primary & secondary/tertiary care. Available from https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/ • General Medical Council. Good practice in prescribing and managing medicines and devices. Shared care. Available from https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/shared-care • NICE NG197: Shared decision making. Last updated June 2021. https://www.nice.org.uk/guidance/ng197/.

Appendix 1: Arrangements for retinal monitoring

York and Scarborough